Publication Types: Case Reports

# Pemphigus vulgaris in oral cavity: Clinical analysis of 71 cases

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Received: 03/01/2008
Accepted: 15/02/2008

**Indexed in:**
-Index Medicus / MEDLINE / PubMed
-EMBASE, Excerpta Medica
-SCOPUS
-Indice Médico Español
-IBECS

Shamim T, Varghese VI, Shameena PM, Sudha S. Pemphigus vulgaris in oral cavity: Clinical analysis of 71 cases. Med Oral Patol Oral Cir Bucal. 2008 Oct1;13(10):E622-6.

http://www.medicinaoral.com/medoralfree01/v13i10/medoralv13i10p622.pdf

## Abstract

Objective: The purpose of the study was to evaluate the clinical presentation of pemphigus vulgaris in the oral cavity. Study design: A retrospective study of 71 cases of pemphigus vulgaris obtained over a period of 7 years from 1st January 2001 to 31st December 2007 in the Department of Oral Pathology, Government Dental College and Department of Dermatology, Government Medical College, Calicut was designed. Clinical details such as age, sex, intraoral distribution, extent of oral lesions, oral presentation, duration, oral involvement (whether primary or secondary) and mode of onset were noted from the files of corresponding Departments. Results: In about 53.52% of cases, the oral cavity was the primary site of involvement. The mean age was 42.73 years and male: female ratio was 1:1.73. The most commonly affected sites were the buccal mucosa and the palate. The disease began with generalized lesions rather than localized lesions. All cases presented as ulcers or erosions.
Conclusion: Although minor differences were noted, the results of this study are in relatively good agreement with the literature with regard to the age, gender, and initial presentation of pemphigus vulgaris.

***Key words:*** *Clinical analysis, pemphigus vulgaris, oral cavity, autoimmune disease.*

## Introduction

Pemphigus is a group of potentially life threatening autoimmune diseases characterized by cutaneous and or mucosal blistering (1). Pemphigus can be classified into 6 types: pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceus, paraneoplastic pemphigus and IgA pemphigus (2). Pemphigus vulgaris is the most common variant showing oral lesions as an initial manifestation in 50% of cases (3). This life threatening illness affects only 1-5 patients per million populations per year (4). The peak incidence of pemphigus vulgaris occurs between the fourth and sixth decades of life with a male to female ratio of 1:2 (5).
Clinically, the oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions (6). While any area in the oral cavity can be involved, the soft palate, buccal mucosa and lips are predominantly affected (6). The diagnosis depends on biopsy confirmation of intraepithelial vesicle formation, acantholysis and the presence of Tzanck cells (7). While the precise pathogenesis of pemphigus vulgaris is not clear, recent studies have shown that acantholysis can occur in the presence of auto antibodies against 9 alpha nicotinic acetylcholine receptor (8).
Demonstration of immunoglobulins especially IgG and complement in the intercellular space by direct immunofluorescence (DIF) is a very reliable test for pemphigus vulgaris (9). Indirect immunofluorescence studies enable a search for circulating auto antibodies in the patient's serum and are usually performed after direct immunofluorescence studies reveal antibody deposits in the mucosa or skin (10).

As the oral mucosa is often the first affected site in most of the cases, Dental professionals plays a critical role in diagnosing and managing oral lesions. The aim of this study was to evaluate the clinical presentation of pemphigus vulgaris in oral cavity.

## Materials and Method

A retrospective study of 71 cases of pemphigus vulgaris obtained over a period of 7 years from 1st January 2001 to 31st December 2007 in the Department of Oral Pathology, Government Dental College, Calicut and Department of Dermatology, Government Medical College, Calicut was designed. The following criteria were used:

A) Inclusion criteria

1. All age groups.
2. Histopathologically confirmed cases of oral pemphigus vulgaris.
3. Reports with adequate case histories.

B) Exclusion criteria

1. Subjects with systemic disorders such as diabetes mellitus, hematologic disturbances.
2. Physically debilitated subjects.

Clinical details like age, sex, intraoral distribution, extent of oral lesions, oral presentation, duration, oral involvement (whether primary or secondary) and mode of onset were noted from the files of corresponding Departments. Histopathologic examination with or without direct immunofluorescence was the method of diagnosis in all cases. Direct immunofluorescence was done for 4 cases. Statistical analysis was executed using Microsoft Excel computer software.

## Results

Age distribution of pemphigus vulgaris was from 15 to 70 years with a mean age of 42.73 years. The youngest patient was 15 years old and the oldest patient was 70 years. Mean age of presentation in men was 47.50 years and in women was 39.75 years. The majority of the patients were in the 41-50 year age group (28.16%). The next highest number of patients was in the age group of 31-40 years (23.94%) followed by the age group of 21-30 years (16.90%) (Figure-1).

Of the 71 patients, the male: female ratio was 1: 1.73. Duration was taken as the period between the time when patient first noticed the oral lesion and the time the patient reported to the hospital. The mean duration of pemphigus vulgaris was 5.5 ± standard deviation of 3.35 months. Nikolsky sign was positive in all cases. In our case series, pemphigus vulgaris began with generalized lesions (53.52%) rather than localized lesions (46.48%).

In about 53.52% of cases, the oral cavity was the primary site of involvement. 16 (22.53%) presented skin lesions initially and 17 (23.94%) presented with simultaneous involvement of the skin and the oral mucosa. Pain was the presenting symptom in the majority of cases (53.52%) followed by burning sensation (46.48%). All cases presented as ulcers or erosions. This was followed by crusted lesions on lip (47.89%). Blistering was evident only in 11 (15.49%) cases.

The buccal mucosa (64, 90.14%) was the most commonly affected site followed by palate and lips (36, 50.70%). This was followed by tongue (20, 28.17%), floor of mouth (17, 23.94%) and gingiva (15, 21.12%) (Figure-2).

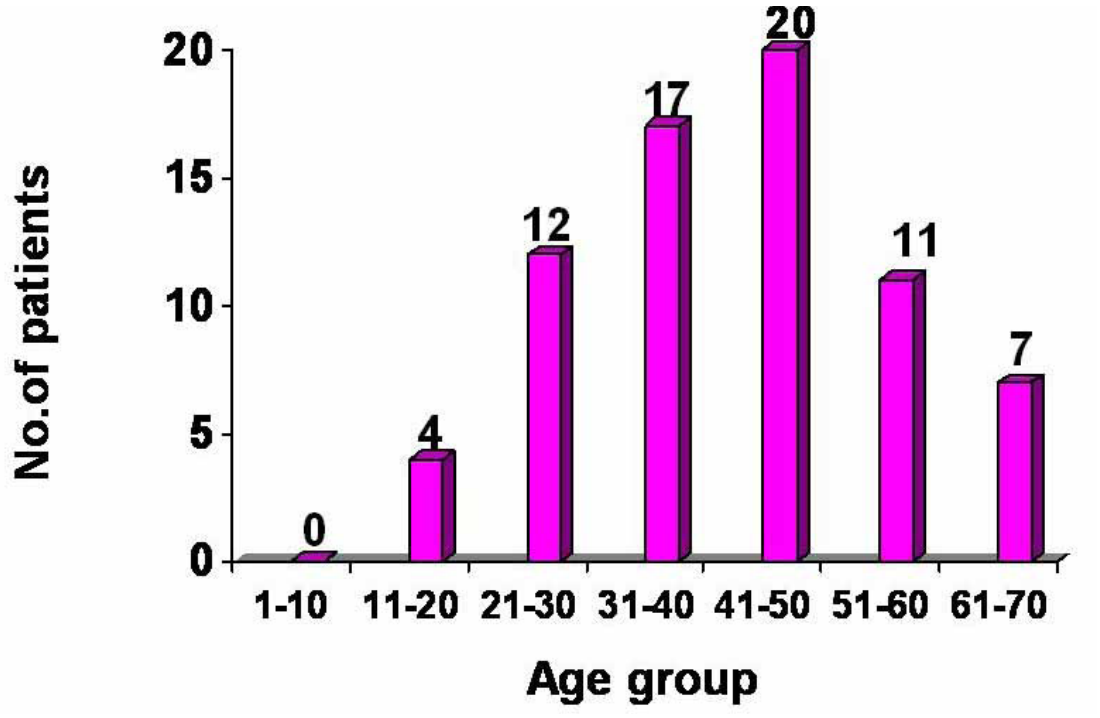


**Fig. 1.** Age distribution of pemphigus vulgaris..

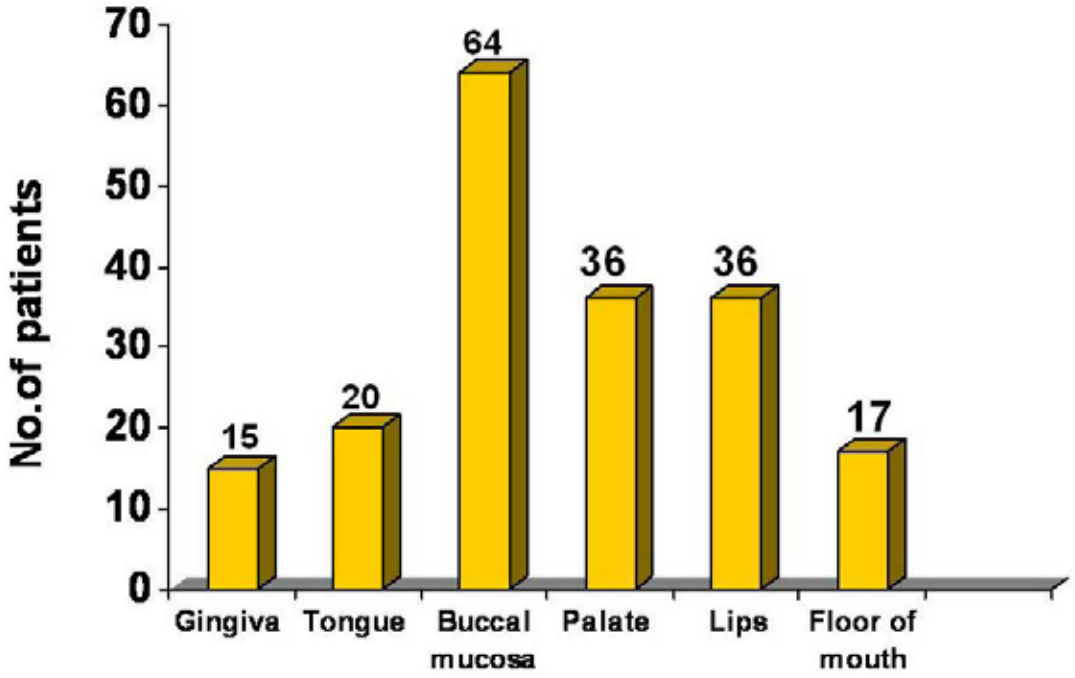


Fig. 2. Distribution of the oral lesions.

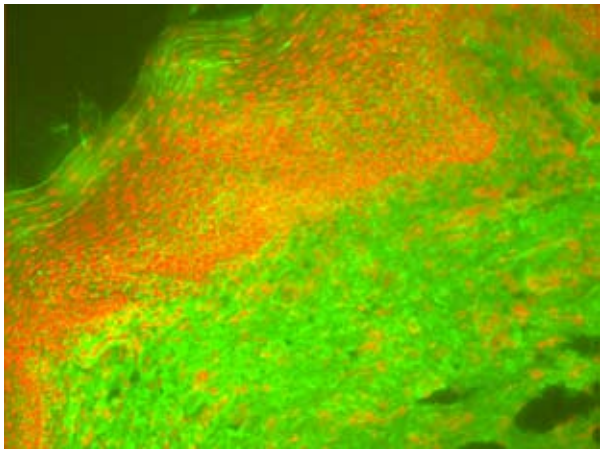

**Fig. 3.** IgG positivity with direct immunofluorescence.

The extent of oral lesion was rated using 3 grades as follows:
Grade I : Only 1 site is involved
Grade II : 2 sites are involved
Grade III : 3 or more sites are involved
About 38 cases (53.53%) were grade III followed by grade II (20 cases, 28.17%) and grade I (13 cases, 18.30%).95% of cases showed parakeratinized epithelium with suprabasilar cleft and acantholytic cells. Tombstone appearance was noted in 50% of cases.
We found 2 cases with sole gingival involvement presenting as chronic desquamative gingivitis in the form of erosions. Direct immunofluorescence was performed in 4 cases. All cases showed fluorescence with IgG and C3. The intensity of fluorescence was moderate with IgG in all cases (Figure-3). One case showed fluorescence with IgM, IgA and fibrinogen.
One of the patients was affected by systemic condition such asThymoma, which would suggest paraneoplastic pemphigus. Fourteen patients showed throat involvement, eight patients showed genital involvement and two patients showed eye involvement. The most common cutaneous sites involved were the trunk (70.42%) followed by scalp (53.52%) and face (39.43%). The majority of the patients were treated with systemic and topical corticosteroids.

## Discussion

In the present study, pemphigus vulgaris (PV) most frequently occurred in patients in the fifth decade. These results are consistent with the previous reports of Iamaroon et al(5) and Camacho-Alonso et al(11). Davenport et al(7) and Sirois et al(12) have found in their studies a mean age of 56.5 years and 56.1 ± standard deviation of 14.9 years respectively(Table-1).In our series, the mean age was 42.73 years. In the present study, no case was detected below 15 years. We also encountered a case of pemphigus vulgaris in a 15- year- old female, presented with burning sensation in buccal mucosa. This was consistent with the finding of Ariyawardana et al (13).
In our study females were affected more frequently with a female to male ratio of 1.73:1.This was in agreement

**Table 1.** Comparison with other studies.

| Parameters | Our study | Shamim et al (3) | Iamaroon et al (5) | Davenport et al (7) | Camacho-Alonso et al (11) | Sirois et al (12) |
|---|---|---|---|---|---|---|
| Number of cases | 71 | 20 | 18 | 33 | 14 | 42 |
| Age group(years) | 15-70 | 20-69 | 18-55 | 27-79 | 21-87 | 27-68 |
| Average age(years) | 42.73 | 42.3 | 37.7 | 56.5 | 44.78 | 56.1 ± standard deviation of 14.9 years |
| Duration(months) | 1-12 | 1-12 | 1-98 | - | 0.75-72 | - |
| Average duration(months) | 5.5± standard deviation of 3.35 | 8 | 12 | - | 11.66 | - |
| Females | 45 | 12 | 12 | 25 | 10 | 30 |
| Males | 26 | 8 | 6 | 8 | 4 | 12 |
| Female:male ratio | 1.73:1 | 3:2 | 2:1 | 3.1:1 | 2.5:1 | 2.5:1 |
| Method of diagnosis | Biopsy and DIF | Biopsy and DIF | Biopsy and DIF | Biopsy and DIF | Biopsy and DIF | Biopsy |
| Treatment | Corticosteroids | - | Corticosteroids and interferon | - | Corticosteroids | - |

**Table 2.** Comparison of distribution of oral lesions in various studies.

| Site of involvement | Our study | Shamim et al(3) | Iamaroon et al(5) | Sirois et al (12) | Laskaris et al (15) | Robinson et al(16) |
|---|---|---|---|---|---|---|
| Buccal mucosa | 64 | 18 | 11 | 18 | 89 | 10 |
| Palate | 36 | 12 | 6 | 3 | 103 | 7 |
| Tongue | 20 | 6 | 4 | 2 | 52 | 10 |
| Lips | 36 | 11 | 3 | - | 89 | 6 |
| Gingiva | 15 | 1 | 17 | 13 | 33 | 11 |
| Floor of mouth | 17 | 2 | 3 | 0 | 16 | 6 |

with the published literature (3,5) (Table-1). But contradictorily, Neville et al (14) found an equal male to female distribution in PV. The discordance in findings may be due to the different geographic and ethnic natures of patients studied.

The duration of presentation of oral lesion was 1 year in the published literature (5) as shown inTable-1. But in our observations, we found an average duration of 5.5± standard deviation of 3.35 months. This short duration of oral presentation may be due to the fact that in most of our cases, the presenting symptom was pain which will alert the patient to seek treatment as soon as possible. The other presenting symptom noted was the burning sensation, which was in accordance with other studies (3, 11).

PV rarely tended to have a sudden onset with severe and widespread lesions. In the study of Laskaris et al (15), 91.4% showed mild onset and lesions remained localized. But in the present study, we found that PV began with generalized lesions (53.52%) rather than localized lesions (46.48%).

It was interesting to note that in our observation it was seen that most of PV have initial oral manifestations (53.52%) followed by simultaneous involvement of skin and the oral mucosa (23.94%) and skin lesions alone (22.53%). This was in line with other studies(5,11).

As the oral cavity is always subjected to minimal trauma and also the roof is very thin it ruptures and forms an extreme area of erosion or ulcer. In our case series, all cases presented as ulcers. This was in agreement with the reports of various authors (11, 12).

In the present study, the extent of oral lesion was rated using Camacho-Alonso et al (11) grading. About 53.52% of cases, grade III involvement was noted and this was consistent with the literature reviewed (3, 11).

With regard to the intraoral distribution of PV, buccal mucosa (90.14%) was the most common site followed by palate, lips (50.74%) and tongue (28.17%). This was in line with the reports of various authors (3, 12). However Robinson et al (16) had found majority of oral lesions in gingiva. Similarly, Laskaris et al (15) found majority of cases in palate (Table-2). In our case series, we found 2 cases with sole involvement of gingiva, presented as chronic desquamative gingivitis in the form of erosions. This condition should be differentiated from desquamative gingivitis resulting from lichen planus and mucous membrane pemphigoid (17, 18).

Since the clinical features of oral pemphigus vulgaris are similar to benign mucous membrane pemphigoid and lichen planus, the diagnosis of pemphigus vulgaris should be confirmed with conventional histology and

immunopathologic studies. The diagnosis of pemphigus vulgaris is based on 3 independent sets of criteria: clinical features, histology and immunological tests (19). This chronic autoimmune cutaneous mucosal disease is often diagnosed late when it is presented only in the oral cavity and the diagnosis is confirmed using pathological examination and direct immunofluorescence (DIF) testing of the healthy perilesional mucosa of patient with pemphigus vulgaris (20).

Histologically, there is an intraepidermal blister associated with acantholytic cells (21). Laskaris (22) and Daniels et al (23) have reported positive direct immunofluorescence for IgG in 100% of cases. The immunoperoxidase proved to be a viable alternative to the use of DIF(24). It may be of particular value to the Oral Pathologist, who is more likely to be dealing with oral PV. In addition, the interpretation does not require specialized microscopy and tissue sections can be stored and retrieved for retrospective study(24). Specific enzyme linked immunosorbent assays (ELISA) are also available for detecting desmoglein 3 and desmoglein 1 auto antibodies(25). In future, the diagnosis and long- term follow up of patients with PV would rely on detecting and quantifying antibodies against desmoglein proteins using ELISA.

Pemphigus vulgaris is generally managed with topical, oral and intralesional corticosteroids (19). The current therapeutic regimen of pemphigus vulgaris is largely based on systemic immunosuppressants such as systemic corticosteroids along with other adjuvants like methotrexate, cyclophosphamide, mycophenolate mofetil and intravenous immunoglobulins (10). Robinson et al (16) emphasized the value of early diagnosis and early treatment on prognosis and the course of pemphigus vulgaris. Drugs such as cholinergic agonists are promising and it will protect the keratinocyte monolayers against anti desmoglein antibody-induced acantholysis and reverse acantholysis produced by pemphigus vulgaris immunoglobulins (8). Plasmin inhibitors such as aprotinin can also prevent the development of acantholysis by inhibiting the conversion of plasminogen into plasmin (8).

## Conclusion

Although minor differences were noted, the results of this study are in relatively good agreement with the literature with regard to the age, gender, and initial presentation of pemphigus vulgaris. Further studies have to be carried out with larger sample sizes to evaluate the clinical nature of oral pemphigus vulgaris.

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***Acknowledgements***

Dr Najeeba Riyaz, Professor and Head and Dr.T.Salim, Senior Lecturer, Department of Dermatology, Government Medical College, Calicut, India for all the help rendered for this study.